Modeling the spread of malaria

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We are developing mathematical models to better understand the transmission and spread of malaria. We model the disease through ordinary differential equations (ODEs) where humans and mosquitoes interact and infect each other. This model is used to determine which factors are most responsible for the spread of malaria.

Malaria is an infectious disease caused by the *Plasmodium* parasite and transmitted between humans through the bite of the female *Anopheles* mosquito. An estimated 40% of the world's population live in malaria endemic areas. It kills about 700, 000 – 2.7 million people a year, 75% of whom are African children. The incidence of malaria has been growing recently due to increasing parasite drug-resistance and mosquito insecticide-resistance. Therefore, it is important to understand the important parameters in the transmission of the disease and develop effective solution strategies for its prevention.

Mathematical modeling of malaria began in 1911 with Ross and major extensions were described by MacDonald in 1957. Recently, Ngwa and Shu [1] proposed an ODE model for the spread of malaria. We analyze a similar model that contains additional immigration for humans. The new model (Figure 1) and the results of our analysis are described in more detail in Chitnis *et al.* [2].

We showed that there exists a domain, $\mathcal{D}$, in the positive cone of $\mathbb{R}^7$ where the model is epidemiologically and mathematically well-posed. Disease-free equilibrium points are steady state solutions where there is no malaria in either the human or mosquito populations. There are two disease-free equilibrium points in $\mathcal{D}$ on the boundary of the positive cone: one with only humans and no mosquitoes, x_{mfe} and one with humans and mosquitoes, x_{dfe}.

We also defined a reproductive number, R_0 (the number of new infections caused by one individual in an otherwise fully susceptible population through the duration of the infectious period), for the model using the next generation operator approach, as described by Diekmann *et al.* in [3].

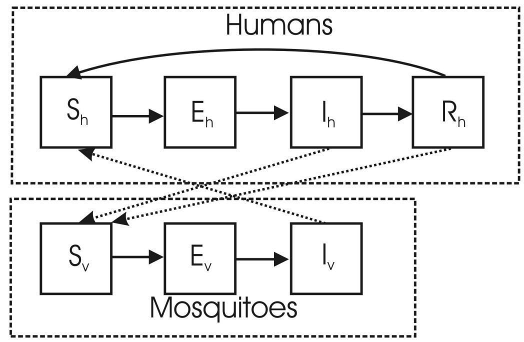

Figure 1: *Schematic of the mathematical model for malaria transmission. The model divides the human population into 4 classes: susceptible, S_h, exposed, E_h, infectious, I_h, and recovered (immune), R_h. Humans enter the susceptible population through birth or immigration. Susceptible humans get infected at a certain probability when they are bitten by infectious mosquitoes. They then progress through the exposed, infectious, and recovered classes, before reentering the susceptible class. Humans leave the population through death and emigration out of all classes, and through additional disease-induced death out of the infectious class. The mosquitoes are divided into 3 classes: susceptible, S_v, exposed, E_v, and infectious, I_v. Mosquitoes enter the susceptible class through birth. Susceptible mosquitoes get infected at a certain probability when they bite infectious or recovered humans (at a lower probability) and then move through the exposed and infectious classes. Both species follow a logistic model for their population growth, with humans having additional immigration and disease-induced death.*

When $R_0 < 1$, x_{dfe} is locally asymptotically stable and the introduction of a small number of infected individuals would not lead to an epidemic. When $R_0 > 1$, x_{dfe} is unstable and the introduction of any infected individual would would lead to an epidemic and malaria persisting in the population.

Endemic equilibrium points are steady state solutions where the disease persists in the population. Using a theorem by Rabinowitz [4] (Thm 1.3), we proved that a positive endemic equilibrium exists for all $R_0 > 1$. Numerical simulations suggest that the endemic equilibrium is stable for $R_0 > 1$ and there is a transcritical bifurcation at $R_0 = 1$ where two branches of equilibrium points intersect and exchange stability (Figure 2). For the special case with no disease-induced death we proved that the bifurcation at $R_0 = 1$ is supercritical (forward) and stable endemic equilibrium points exist for $R_0 > 1$. For some large (though still realistically feasible) values of the disease-induced death rate, there exists a subcritical (backward) bifurcation at $R_0 = 1$ where stable positive endemic equilibrium points exist for $R_0 < 1$. Thus even when $R_0 < 1$, malaria can persist in the population in the presence of a locally asymptotically stable disease-free equilibrium point.

We compiled two reasonable sets of values for the parameters in the model: one for areas of high transmission ($R_0 = 7.0$) and one for areas of low transmission ($R_0 = 1.1$). We numerically computed the sensitivity indices of the reproductive number and the endemic equilibrium to the parameters. In both high and low transmission areas, R_0 is most sensitive to the number of bites on humans per mosquito per day. In areas of low transmission, the equilibrium fraction of infectious humans, i_h, is also most sensitive to the mosquito biting rate. In areas of high transmission, as most people are either infectious or recovered, the most sensitive parameters for i_h are the rates of movement out of the infectious and recovered classes.

The sensitivity indices allow us to compare

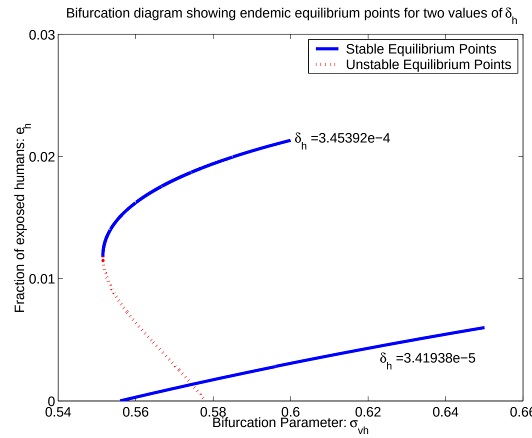

Figure 2: *Two bifurcation diagrams showing the fraction of exposed humans, e_h, in the endemic equilibrium point against the mosquito biting rate, σ_{vh}, for two different values of the disease-induced death rate, δ_h. The curve labelled $\delta_h = 3.45392e-4$ shows a subcritical bifurcation while the one labelled $\delta_h = 3.41938e-5$ shows a supercritical bifurcation.*

the effectiveness of different control strategies, as each strategy affects different parameters to different degrees. Our results agree with field studies that suggest that methods that reduce human-mosquito contact, such as the use of insecticide-treated bed nets, are effective in controlling the spread of malaria [5].

Acknowledgements

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References

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